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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,078	07/21/2005	Michinori Kohara	382.1047	7140
23280 7590 11/10/2008 Davidson, Davidson & Kappel, LLC 485 7th Avenue 14th Floor New York, NY 10018				
EXAMINER				
PITRAK, JENNIFER S				
ART UNIT		PAPER NUMBER		
1635				
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11/10/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/543,078

Applicant(s)

KOHARA ET AL.

Examiner

JENNIFER PITRAK

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-12, 14-16 and 18 is/are pending in the application.
- 4a) Of the above claim(s) 9, 10, 14 and 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7, 8, 11, 12, 16 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/888)
Paper No(s)/Mail Date 10/17/07.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Remarks

Applicant's responded to the 09/17/2007 Office action with claim and specification amendments and arguments filed 03/19/2008. The claim amendments were non-compliant with 37 CFR 1.121. Applicant filed a new set of amended claims on 08/01/2008. The claims filed 08/01/2008 and the arguments filed 03/19/2008 have been considered for this Office Action.

Claims 1-6, 13, and 17 are cancelled. Claim 18 is new. Claims 7-12, 14-16 and 18 are pending. Claims 9, 10, 14, and 15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/30/07. Claims 7, 8, 11, 12, and 18 are under examination insofar as they are directed to elected SEQ ID NO: 23.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification – objection maintained

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see, for example, at least line 22 on p. 16 of the specification). Applicant is required to delete all embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

Claim Objections - withdrawn

The amendments to the claims have obviated the objection of claim 8. Therefore the objection is withdrawn.

Claim Rejections - 35 USC § 112 - withdrawn

The amendments to the claims have obviated the rejection of claim 5 under 35 U.S.C. 112, second paragraph, as being indefinite. Therefore the rejection is withdrawn.

Claim Rejections - 35 USC § 102 - withdrawn

The amendments to the claims have obviated the rejection under 35 U.S.C. 102(b). Therefore, the rejection is withdrawn. Wakita, *et al.* (1999, J. Med. Virol., v.57:217-222).

Claim Rejections - 35 USC § 103-maintained

Claims 7, 8, 11, 12, 16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seki, *et al.* (1994, CA2104649), Bass (2001, Nature v.411:428-429), and Yu, *et al.* (2002, PNAS, v.99:6047-52).

The claims are to an siRNA having a nucleotide sequence of SEQ ID NO: 23 or to a vector that expresses the siRNA. The claims are also to an siRNA having a nucleotide sequence complementary to a sequence of SEQ ID NO: 23. It is noted that an siRNA

Seki, *et al.*, teach an antisense nucleotide targeting HCV and complementary to SEQ ID NO: 23 and that is 20 nucleotides in length. Seki, *et al.* disclose antisense oligonucleotides useful as antiviral agents (see abstract) and particularly disclose SEQ ID NO: 83, which is

complementary to nucleotides 2-20 of the instant SEQ ID NO:23. Seki, *et al.* do not teach siRNAs. Seki, *et al.* do not teach siRNAs in vectors.

Bass teaches on page 429, first column, that RNA interference is a routinely used gene silencing technique that has proven to be more robust than antisense techniques by working more often, decreasing expression to lower levels than antisense oligonucleotides, and working at concentrations several orders of magnitude below the concentrations typically used in antisense experiments.

Yu, *et al.* teach that siRNAs can be expressed from a vector (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to make an siRNA (double-stranded RNA) targeting the region of HCV corresponding to SEQ ID NO:23 for the purpose of reducing HCV expression and to express the siRNA from a vector. Seki, *et al.* teach antisense oligonucleotides that target a nucleotide sequence of the instant SEQ ID NO: 23. Bass provides a motivation to make a double-stranded RNA instead of an antisense oligonucleotide by teaching that RNA interference is more robust than antisense techniques by decreasing expression to lower levels and working at much lower concentrations than antisense. Based on the motivation provided by Bass to use double-stranded RNA instead of antisense compounds to down-regulate target gene expression, one of ordinary skill in the art would recognize that targeting HCV with an siRNA corresponding to SEQ ID NO:23 would be a more effective antiviral agent than just the antisense taught by Seki, *et al.* One of ordinary skill in the art would have had a reasonable expectation of success in making and using an siRNA to reduce HCV expression because Bass teaches RNAi using dsRNA is a more specific and more potent method than antisense. Yu, *et al.* teach that siRNAs can be expressed from vectors. Thus, the

invention of claims 7, 8, 11, 12, 16, and 18 would have been obvious, as a whole, at the time of the invention.

Response to arguments

Applicant argues that because Bass does not compare the effects of antisense oligonucleotides and siRNAs targeting the same sequence, that therefore, one of skill in the art would not have had a reason to use SEQ ID NO: 23 as an siRNA. Applicant also argues that SEQ ID NO: 83 of Seki, et al. is referred to as one of the preferred antisense compound but is excluded from the most preferred antisense compounds, and as such, one of skill in the art would not expect that the siRNA having a sequence complementary to SEQ ID NO: 83 of Seki, et al. to strongly inhibit replication of HCV. This is not persuasive because Seki's antisense oligonucleotide was effective to inhibit HCV and did so well enough to be included in the list of preferred oligonucleotides and Bass teaches that siRNAs are more effective than antisense oligonucleotides. It is agreed that given no sequence from which to begin, one of skill in the art may not arrive at an siRNA targeting the instant SEQ ID NO: 23 from the teachings of Bass alone. However, Seki, et al. clearly provide a target sequence on which to base siRNA design. Given that the antisense oligonucleotides of Seki, et al. functioned to inhibit HCV and that Bass teaches siRNAs as an improvement over antisense oligonucleotides, one of skill in the art would clearly recognize that an siRNA targeting a known functional antisense target would likely result in at least as good of a result, if not a better result.

Finally, Applicant states that neither Seki, et al. nor Bass teach siRNAs having SEQ ID NO: 23 that strongly inhibit replication of HCV. This statement has been addressed in the above response to arguments.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635

/Tracy Vivlemore/
Primary Examiner, Art Unit 1635